

Risk Assessment of Cutaneous Leishmaniasis and the Outcome of Therapy among Patients in Almaza Fever Hospital

Ahmed Omar¹, Mohamed Abd-elsalam el-gohari¹, Nader Nemr², Mohamed aboelmagd²

¹Almaza Fever Hospital, Cairo, Egypt.

²Endemic and Infectious Diseases Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.

Corresponding Author
Ahmed Omar

Mobile:

+201111821665

Email:

PGS.000935113@med.suez.edu.eg

© 2024 The author (s).
Published by Zagazig
University. This is an
open access article
under the CC BY 4.0
license

<https://creativecommons.org/licenses/by/4.0/>.

Receive

date:16/6/2024

Revise date:12/7/2024

Accept date:25/7/2024

Publish date:3/8/2024

Keywords:Leishmaniasis,
Cryotherapy,
Pentostam

Background and study aim:

Leishmaniasis infection was listed by the WHO among the six most important tropical diseases, being endemic in many different countries worldwide with global estimate of 350 Million individuals at risk. It was reported more than 12 million chronic cases worldwide. The aim of this study was to improve disease outcome and disease long term sequelae.

Patients and Methods: This descriptive, cross-sectional study was conducted at Almaza Fever Hospital from December 2020 to December 2021 on 90 patients with cutaneous leishmaniasis diagnosed by clinical examination and direct smear biopsy among military groups in Egypt. Patients who were diagnosed with cutaneous leishmaniasis were given sodium stibogluconate (Pentostam) (20 mg Sb/kg/day (maximum 850 mg) IV/IM for 20-28 days) and Cryotherapy sessions

(Patients received cryotherapy every two weeks for maximum of three months). Follow up examinations were scheduled at the time of cryotherapy). Patients were followed up for reporting any adverse effects.

Results: Upon comparison the outcome of the two treatment modalities, there were 69.1% improved, 5.5% relapsed, 9.1% had treatment failure, 16.4% developed chronic infection among Cryotherapy. While there were 77.1% improved, 5.7% relapsed, 6.7% had treatment failure, 8.6% developed chronic infection. **Conclusion:** Leishmaniasis is common among young males. The results of the treatment of patients with cutaneous leishmaniasis with cryotherapy and Pentostam were comparable.

INTRODUCTION

Leishmaniasis, a common parasitic infection being caused by kinetoplast protozoan parasites of the genus *Leishmania*, is considered a neglected infectious disease. It has posed significant health challenges in numerous tropical and subtropical areas globally. In 98 countries, this disease is prevalent and considered an endemic disease and poses a grave risk to roughly 310 million individuals residing in the affected regions [1].

This disease is a significant issue in developing and underdeveloped nations, especially in the Americas where it is widespread. The main risk factors, stemming from local social, economic, and environmental processes, greatly increase the population at risk of infection [2].

The medical complexity of leishmaniasis leads to a lack of

comprehensive tools and guidelines for managing cases, whether for initial clinical suspicion, diagnoses, treatment or post-therapy follow-up. Existing resources are often limited to specific regions. As a result, leishmaniasis is not given due recognition or priority in public health policy, and its reported awareness does not accurately reflect its true impact [3].

Leishmaniasis is considered a zoonotic disease, with animal vectors being responsible for transmitting the parasites that cause the majority of its forms. However, there have been reports of some forms being transmitted directly between humans [4].

Due to the remote residence of the majority of affected patients and their poor access to health care services,

leishmaniasis has still been considered as a hidden problem and underestimated [5]. There is currently a lack of cost-effective and easy-to-use medications for treating leishmaniasis. Leishmaniasis was not considered a direct threat to industrial countries until it appeared as a co-infection of HIV/AIDS [5].

Chemoprophylaxis or vaccination against various forms of leishmaniasis is not officially recognized or reliable. Regrettably, chemotherapy is still unsatisfactory in many aspects [6].

The current study is designed aiming to improve disease outcome and disease long term sequela via assessment of cutaneous Leishmaniasis therapy outcome among patients attending Almaza fever Hospital.

PATIENTS/MATERIALS AND METHODS

Following the declaration of Helsinki and after approval of Research Ethics Committee of Faculty of Medicine, Suez Canal University, this descriptive, cross-sectional study was conducted at Almaza Fever Hospital from December 2020 to December 2021 on 90 patients with cutaneous leishmaniasis diagnosed by clinical examination and direct smear biopsy among military groups in Egypt. Patients with definitive skin lesion according to clinical and laboratory data were included into the study. Patients were excluded from the study if they refused to share in the study. An informed written consent was a main prerequisite that was obtained from all recruited patients.

This study included control group of 20 healthy participants, age and sex matched with cases presented to the hospital. We included all patients with cutaneous leishmaniasis whom were presented to the hospital from December 2020 to December 2021.

The studied patients were subjected to the following:

1) Structured questionnaire: identifying the environmental factors favoring leishmaniasis spread. The questionnaire was formed of two main parts. *First part:* included demographic data as (age, sex, job, education level, stay length). *Second part:* included the description of living and working environment including land, building, and vegetation, and water collection,

presence of insect-vector and animal-reservoir).

2) Present history of present illness (main complaint, lesion discovery, diagnosis, treatment type and duration, and outcome.

3) Clinical description of skin lesion features such as (type, size, site, number, complication).

4) Patients who were diagnosed with cutaneous leishmaniasis were given sodium stibogluconate (Pentostam) (20 mg Sb/kg/day (maximum 850 mg) IV/IM for 20-28 days) or Cryotherapy sessions (cryotherapy was used every two weeks for maximum of three months. To reduce visits and simplify the follow up process, follow up examinations were scheduled during the same time of cryotherapy). Patients were allocated to which treatment according to feasibility of repeated visits for cryotherapy sessions.

5) Patients were followed up for incidence of adverse effects such as gastrointestinal upset, cardiac affection in form of ECG changes, headache, malaise, hepatotoxicity, coughing and retrosternal pain, fever, sweating, any spontaneous bleeding, skin rash, pain and thrombosis on intravenous administration, or painful intramuscular injection. Treatment failure was considered after 1 month of treatment without resolution of the cutaneous lesions. Failed cases were followed up after another one month for possibility of self-limited resolution and if no change was reported the same treatment was re-administered.

Statistical analysis was done using SPSS version 25 (SPSS Inc., Chicago, IL, USA). Quantitative data were presented as means \pm SD while qualitative data were presented as numbers and percentages (%). Student *t* test was used to test significance of difference for quantitative variables and Chi Square was used to test significance of difference for qualitative variables. A probability value of *p*-value $<$ 0.05 was considered statistically significant.

RESULTS

This study included 90 patients with cutaneous leishmaniasis among military groups in Egypt (Cases) and 20 healthy participants coming to hospital with their siblings (Controls). A total of 90 patients (Cases) and 20 controls participated in our study aged from 21 to 35 years and 20 to 39 years with mean age of 23.9 ± 4.5 years and

25.5± 5.6 years respectively with no significant difference. The BMI was ranging from 22 to 31 and 19 to 29 with a mean BMI 25.8± 2.5 and 23.7± 2.6 Kg/ m² respectively with no significant difference. The most of our participants 97.8% and 95% were males and there were 2.2% and 5% females respectively with no significant difference. Regarding education, 77.8% and 75% was highly educated and 22.2% and 25% was primary and secondary educated respectively with no significant difference. There were 38.9% and 40% from rural areas while 61.1% and 60% from urban areas respectively with no significant difference. There were 7.8% and 10% had chronic diseases

among them 2.2% and 5% diabetic, 4.5% and 5% hypertensive and 1.1% and 0 had cardiovascular diseases. While 92.2% and 90% had no chronic diseases respectively with no significant difference. There were 93.3% and 90% were military workers and 6.6% and 10% were non-military workers among cases and controls respectively with no significant difference. There were 42.2% and 40% non-smokers, 35.6% and 35% current smoker, and 22.2% and 25% Ex-smoker among cases and controls respectively with no significant difference. (**Table1**)

Table 1. Sociodemographic data of patients:

		Cases (n=90)	Controls (n=90)	p-value
Age (years)	Mean ± SD	23.9± 4.5	25.5± 5.6	0.460a
	Median (range)	26.5 (21, 35)	25.5 (20, 39)	
BMI (Kg/m ²)	Mean ± SD	25.8± 2.5	23.7± 2.6	0.152a
	Median (range)	25 (22, 31)	24 (19, 29)	
Gender	Male , n(%)	88 (97.8)	19 (95)	0.200b
	Female n(%)	2 (2.2)	1 (5)	
Education	Highly educated	70 (77.8)	15 (75)	0.311c
	Primary and secondary education, n (%)	20 (22.2)	5 (25)	
Residence	Rural, n (%)	35 (38.9)	8 (40)	0.410c
	Urban, n (%)	55 (61.1)	12 (60)	
Chronic diseases	No, n (%)	83 (92.2)	18 (90)	0.112b
	Yes, n (%)	7 (7.8)	2 (10)	
	Diabetes, n (%)	2 (2.2)	1 (5)	
	Hypertension, n (%)	4 (4.5)	1 (5)	
	Cardiovascular, n (%)	1 (1.1)	0 (0)	
Occupation	Non-Military workers, n (%)	6 (6.6)	2 (10)	0.060b
	Military) workers, n (%)	84 (93.3)	18 (90)	
Smoking	Non-smoker, n (%)	38 (42.2)	8 (40)	0.866c
	Current smoker, n (%)	32 (35.6)	7 (35)	
	Ex-smoker, n (%)	20 (22.2)	5 (25)	

BMI: Body Mass index, SD: standard deviations, n (%) number (percentage out of total)

Upon assessing the characteristics of the lesions among the cases, the lesions were disseminated among 72.2% while it was localized among 27.8%. The number of lesions was ranging from 1 to 25 lesions with the mean 5.5± 3.5. The size of lesions was ranging from 1 to 5 cm with mean 1.3± 0.6 cm. (**Table2**)

Table 2. Characteristics of the lesions among the participants:

		Cases (N=90)
Type of lesion	Disseminated, n (%)	65 (72.2)
	Localized, n (%)	25 (27.8)
Number of lesions	Mean \pm SD	5.5 \pm 3.5
	Median (Range)	6 (1, 25)
Size of lesions (cm)	Mean \pm SD	1.3 \pm 0.6
	Median (Range)	1 (1, 5)

N: total number of studied patients, SD: standard deviations, n (%) number (percentage out of total)
 N.B: Quantitative data represented as mean \pm SD Qualitative data represented as frequency (percentage)

The treatment used was cryo-therapy among 61.1% and Pentostam among 38.9%. (table 3)

Table 3: Treatment used among the participants:

		N=90
Treatment	Cryo-therapy, n(%)	55 (61.1%)
	Pentostam, n(%)	35 (38.9%)

N: total number of study patients, n (%) number (percentage out of total)

Regarding treatment effects among the participants after first session of treatment, 92.2% had erythema, 95.6% had induration, 14.4% developed ulcer. After second session, 90% had erythema, 92.2% had induration, 15.6% developed ulcer. (table 4)

Table 4: Treatment effects after first and second session among the participants.

first session		N=90	second session		N=90
Erythema	Yes, n(%)	83 (92.2)	Erythema	Yes, n(%)	81 (90)
	No, n(%)	7 (7.8)		No, n(%)	9 (10)
Induration	Yes, n(%)	86 (95.6)	Induration	Yes, n(%)	83 (92.2)
	No, n(%)	4 (4.4)		No, n(%)	7 (7.8)
Ulcer	Yes, n(%)	13 (14.4)	Ulcer	Yes, n(%)	14 (15.6)
	No, n(%)	77 (85.6)		No, n(%)	76 (84.4)

N: total number of the studied cases, n (%) number (percentage out of total)
 N.B: Qualitative data represented as frequency (percentage)

Regarding outcome of treatment, there were 72.2% improved, 5.6% relapsed, 8.9% had treatment failure, 13.3% developed chronic infection. Discontinuation of treatment in these patients might be an explanation for this loss of efficacy. (table 5)

Table 5: Outcome of treatment among the treatment.

		Cases (N=90)
Improvement	Yes, n (%)	65 (72.2)
	No, n (%)	25 (27.8)
Relapse	Yes, n (%)	5 (5.6)
	No, n (%)	85 (94.4)
Treatment failure	Yes, n (%)	8 (8.9)
	No, n (%)	82 (91.1)
Chronic	Yes, n (%)	12 (13.3)
	No, n (%)	78 (86.7)

N: total number of the studied cases, n (%) number (percentage out of total)
 N.B: Qualitative data represented as frequency (percentage)

Upon comparison the outcome of the two treatment modalities, there were 69.1% improved, 5.5% relapsed, 9.1% had treatment failure, 16.4% developed chronic infection among Cryo-therapy, while

there were 77.1% improved, 5.7% relapsed, 6.7% had treatment failure, 8.6% developed chronic infection among pentostam group with no statistically significant difference. (**table 6**)

Table 6: Comparison of outcome between the two treatment modalities.

		Cryotherapy n= 55	Pentostam n= 35	p value
Improvement	Yes, n (%)	38 (69.1)	27 (77.1)	0.310
	No, n (%)	17 (30.9)	8 (22.9)	
Relapse	Yes, n (%)	3 (5.5)	2 (5.7)	0.980
	No, n (%)	52 (94.5)	33 (94.3)	
Treatment failure	Yes, n (%)	5 (9.1)	3 (6.7)	0.600
	No, n (%)	50 (90.9)	42 (93.3)	
Chronic	Yes, n (%)	9 (16.4)	3 (8.6)	0.105
	No, n (%)	46 (83.6)	32 (91.4)	

n (%) number (percentage out of total)

N.B: QUALITATIVE DATA REPRESENTED AS FREQUENCY (PERCENTAGE)

DISCUSSION

This descriptive, cross-sectional study conducted on patients with cutaneous leishmaniasis among military groups in Egypt. Patients were recruited from the military and infectious diseases hospital from December 2020 to December 2021.

This study main objectives were to study the prevalence of cutaneous leishmaniasis among military groups, identify the ecological factors favoring its spread and to describe the lines of proper prevention and management of that disease.

In this study upon assessing the characteristics of the lesions among the participants, the lesions were disseminated among 72.2% while it was localized among 27.8%. The number of lesions were ranging from 1 to 25 lesions with the mean 5.5 ± 3.5 . The size of lesions was ranging from 1 to 5 cm with mean 1.3 ± 0.6 cm. Similarly, a study by Bahnan et al., [7] showed that the mean number of lesions was 1.7 with 0.5 standard deviation and the mean size of lesions was 25 X19 cm.

A study by Goncalves and Costa, [2018] conducted a noncomparative open clinical trial among 15 patients. They have reported that more than 50% of their patients had only one lesion, and only single patient have been found to have three lesions [8].

In this study, after first session of treatment, 92.2% had erythema, 95.6% had induration, 14.4% developed ulcer. After second session of treatment, 90% had erythema, 92.2% had induration, 15.6% developed ulcer. Similarly, a study by Goncalves and Costa, [8] have also reported pain, itch and burning sensation to be

the most commonly incident side effects. Only one of their patients developed skin blisters on the treatment site.

In this study regarding outcome of treatment, there were 72.2% improved, 5.6% relapsed, 8.9% had treatment failure, 13.3% developed chronic infection. No treatment response could be due to patient factors, compositions of the applied treatment and parasite factors. Another important and serious factor that affect treatment response if drug resistance.

Similar to our results, a study by Bamorovat et al., [9] aimed to investigate the role of demographic, clinical and ecological risk factors for unresponsive treatment, incidence of relapse and chronicity to patients with successful treatment for cutaneous leishmaniasis. They have found that 6.5% of their patients showed relapse with treatment failure among 11.2% and chronicity among 6.2%.

In agreement with our results, Omidian et al., [6] found that the improvement was among 100% of the participants and scars developed among 16.7% of the participants treated by Cryotherapy.

This goes in line with a study by Navas et al., [10] conducted among sixty patients. The results showed that after standard of care treatment, 63% of participants were clinically cured [n =38], while 22 presented treatment failure which was determined 13 weeks after initiation of treatment.

In their study, Goncalves and Costa, [8] have reported that only two [25%] of the eight untreated lesions did not progress to cure without the need of thermotherapy and 18 of the treated 21 lesions progressed to cure after the treatment.

One patient did not achieve cure after three months of follow-up.

The results of a recent case report of 3 cases were remarkable, and the CL wound healing in MT was faster than routine therapies [11]. Similarly, Polat et al., [12] have treated 29 patients with Glucantimeresistant/tolerant cutaneous leishmaniasis wounds with *L. sericata* larvae and its larval secretions efficiently without leaving any scar tissues without any PCR-detection of *Leishmania* spp 1-2 months after treatment.

In this study, upon comparison the outcome of the two treatment modalities, there were 69.1% improved, 5.5% relapsed, 9.1% had treatment failure, 16.4% developed chronic infection among Cryo-therapy. While there were 77.1% improved, 5.7% relapsed, 6.7% had treatment failure, 8.6% developed chronic infection. There was no significant difference between outcomes of the two treatment modalities. This study conducted among 90 patients aged from 21 to 35 years with mean age of 23.9 ± 4.5 years. Similar to our results, a study by Omidian et al., [6] who investigated the effect of Nd:YAG laser therapy [NDY] on cutaneous leishmaniasis in comparison with meglumine antimoniate have shown comparable results between both treatment modalities.

This may be due to conducting this study among military groups. In agreement with our results, Leishmaniasis was common more among males [72%] in a study by Bahnan et al., [7] among participants with the mean age 32.38 ± 15.05 years.

This goes in line with Navas et al., [10] who revealed that Leishmaniasis common among young male who included in their study.

Another study by Abdellahi et al., [13] found that among 150 leishmaniasis patients 91 males and 59 females with mean age of 33 ± 18 years. In this study, regarding education, 77.8% was highly educated and 22.2% was primary and secondary educated. There were 7.8% had chronic diseases while 92.2% had no chronic diseases.

In a similar study by Abdellahi et al., [13] demonstrated that the majority of participants in treatment groups had low educational levels. This study had limitations as short follow up period and its nature as a descriptive cross-sectional study. Therefore, intensive research

should be performed in clinical fields to achieve desired results.

CONCLUSION

leishmaniasis is common among young males. The results of the treatment of patients with cutaneous leishmaniasis with each of cryotherapy and Pentostam were effective. Larger scale study is recommended as well as longer duration of follow-up for more investigation of the treatment modality.

Funding: None. Author funded

Conflict of Interest: None.

Author contribution: We declare that all listed authors have made substantial contributions to all of the following three parts of the manuscript:

- Research design, or acquisition, analysis or interpretation of data;
- drafting the paper or revising it critically;
- approving the submitted version.

We also declare that no-one who qualifies for authorship has been excluded from the list of authors.

Ethical consideration: Permission and official approval to carry out the study was obtained. All patients signed a written informed consent before inclusion into this study and the institutional ethical committee at Sue Canal University, Faculty of Medicine approved the study (approval number 4608 dated 29#6#2021). The study protocol conforms with the ethical guidelines of the 1975 Declaration of Helsinki.

HIGHLIGHTS:

- Cutaneous leishmaniasis is common among young males.
- Treatment of patients with cutaneous leishmaniasis with each of cryotherapy and Pentostam were effective.

REFERENCES

1. Glans H, Dotevall L, Söbirk SK, Färnert A, Bradley M. Cutaneous, mucocutaneous and visceral leishmaniasis in Sweden from 1996-2016: a retrospective study of clinical characteristics, treatments and outcomes. *BMC Infect Dis* 2018; 18(1): 632.

2. Amorim CF, Novais FO, Nguyen BT, Mistic AM, Carvalho LP, Carvalho EM, et al. Variable gene expression and parasite load predict treatment outcome in cutaneous leishmaniasis. *Sci Transl Med* 2019; 11(519): 4204.
3. Karam, TK, Ortega S, Nakamura T, Auzély-Velty R, & Nakamura CV. Development of chitosan nanocapsules containing essential oil of *Matricaria chamomilla* L for the treatment of cutaneous leishmaniasis. *International Journal of Biological Macromolecules* 2020; 162, 199-208.
4. Chakravarty J, and Sundar, S. Current and emerging medications for the treatment of leishmaniasis. *Expert Opinion on Pharmacotherapy* 2019; 20(10): 1251-1265.
5. Bullón J, Márquez L, Fernández JA, Scorza C, Scorza JV, Rodríguez J, et al. A Promising Cutaneous Leishmaniasis Treatment with a Nanoemulsion-Based Cream with a Generic Pentavalent Antimony (Ulamina) as the Active Ingredient. *Cosmetics*. 2021; 8(4):115.
6. Omidian M, Jadbabaei M, Omidian E, Omidian Z. The effect of Nd:YAG laser therapy on cutaneous leishmaniasis compared to intralesional meglumine antimoniate. *Postepy Dermatol Alergol* 2019; 36(2): 227-231.
7. Bahnan BA, Shabu SA, and Sleman SA. Intralesional pentostam versus intralesional metronidazole in treating cutaneous leishmaniasis: a comparison study. *Zanco Journal of Medical Sciences (Zanco J Med Sci)* 2019; 23(2): 257-263.
8. Goncalves S, and Costa, C. Treatment of cutaneous leishmaniasis with thermotherapy in Brazil: an efficacy and safety study. *Anais Brasileiros de Dermatologi* 2018; 93: 347-355.
9. Bamorovat M, Sharifi I, Dabiri S, Shamsi Meymandi S, Karamoozian A, Amiri R, et al. Major risk factors and histopathological profile of treatment failure, relapse and chronic patients with anthroponotic cutaneous leishmaniasis: A prospective case-control study on treatment outcome and their medical importance. *PLoS Negl Trop Dis*. 2021 Jan 28;15(1):e0009089.
10. Navas A, Fernández O, Gallego-Marín C, Castro MDM, Rosales-Chilama M, Murillo J, et al. Profiles of Local and Systemic Inflammation in the Outcome of Treatment of Human Cutaneous Leishmaniasis Caused by *Leishmania* (Viannia). *Infect Immun* 2020; 88(3): e00764-19.
11. Nasiri A, Jahanifard E, Sharififard M, Arjmand R, Rasai S, Haeri T. Maggot Debridement Therapy (MDT) for Treatment of Cutaneous Leishmaniasis Wound using *Lucilia serricata* Larvae in Iran: Case Reports. *J Adv Med Biomed Res* 2022; 30 (138) :69-72
12. Erdal P, Zekayi K, Serhat S. Treatment of Glucantime-resistant/tolerant cutaneous leishmaniasis with *Lucilia sericata* larvae and its larval secretions: The first study in the world. *Trop Biomed* 2016 Dec 1;33(4):668-674.
13. Abdellahi L, Hejazi SH, Amirmozafari N, Sotoodehnejadnematalahi F. Comparison of Three Different Therapies for Cutaneous Leishmaniasis and Identification of the Etiologic Isolates in Isfahan, Iran. *Arch Iran Med* 2020; 23(11):740-748.

Site as: Omer, A., el-gohari, M., Nemr, N., Aboelmagd, M. Risk Assessment of Cutaneous Leishmaniasis and the Outcome of Therapy among Patients in Almaza Fever Hospital. *Afro-Egyptian Journal of Infectious and Endemic Diseases*, 2024;14(3):342-348. doi: 10.21608/aeji.2024.289905.1389